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Mapping cancer research across Central & Eastern Europe, the Russian Federation and Central Asia: implications for future National Cancer Control Planning.

Mursheda Begum^, Grant Lewison, Jacek Jassem, Vlad Mixich, Tanja Cufer, Talgat Nurgozhin, Pavel Shabalkin, Tezer Kutluk, Zoltan Voko, Davorin Radosavljevic, Eduard Vrdoljiak, Alexandru Eniu, Jan Walewski, Ajay Aggarwal, Mark Lawler* and Richard Sullivan*.

Corresponding author: Mursheda Begum MSc, Institute of Cancer Policy, Cancer Epidemiolsogy, Population & Global Health, School of Cancer Sciences, King's College London mursheda.begum@kcl.ac.uk

Grant Lewison, PhD, Institute of Cancer Policy, Cancer Epidemiology, Population & Global Health, School of Cancer Sciences, King's College London grant.lewison@kcl.ac.uk

Vlad Mixich MD Romanian Health Observatory, Bucharest, Romania, vlad.mixich@health-observatory.ro

Prof Tanja Cufer, MD, PhD, University Clinic Golnik. Medical Faculty Ljubljana, Slovenia; tanja.cufer@klinika-golnik.si

Prof Talgat Nurgozhin MD PhD, Center for Life Sciences "National Laboratory Astana" PI, Nazarbayev university, Astana, Kazakhstan tnurgozhin@nu.edu.kz

Prof Jacek Jassem MD PhD, Medical University of Gdansk, Dept. of Oncology and Radiotherapy, Gdansk, Poland jjassem@gumed.edu.pl

Prof Pavel Shabalkin MD, Secretary of the Federal Oncology commission of the Ministry of Health of Russia, Moscow, Russia. p.shabalkin@gmail.com

Prof M. Tezer Kutluk, MD. PhD. FAAP. Hacettepe University Faculty of Medicine and Cancer Institute, Department of Pediatric Oncology, 06100 Ankara-Turkey, tezer kutluk@gmail.com

Prof. Zoltán Vokó MD PhD DSc, Department of Health Policy & Health Economics, Eötvös Loránd University, & Syreon Research Institute, Budapest, Hungary, zoltan.voko@syreon.eu

Prof Davorin Radosavljevic MD PhD, Department of Medical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia and Montenegro radosavljevici@yahoo.com

Prof Eduard Vrdoljiak MD, PHD Department of Oncology, Clinical Hospital Center Split, School of Medicine, University of Split, Split, Croatia. email: edo.vrdoljak@gmail.com

Prof Jan Walewski, MD Maria Sklodowska-Curie Institute Oncology Center, Warszawa, Poland Jan.Walewski@coi.pl

Prof Alexandru Eniu, MD, PhD, Cancer Institute “Ion Chiricuta”, Cluj-Napoca, Romania, leniu@iocn.ro

Ajay Aggarwal MD, PhD, Institute of Cancer Policy, Cancer Epidemiology, Population & Global Health, School of Cancer Sciences, King’s College London & Guy’s & St.Thomas’ NHS Trust, London ajay.aggarwal@kcl.ac.uk

Prof Mark Lawler MD PhD, Centre for Cancer Research and Cell Biology, Queen’s University Belfast, 97 Lisburn Rd, Belfast, BT9 7AE, UK mark.lawler@qub.ac.uk

Prof Richard Sullivan MD PhD, Institute of Cancer Policy, Cancer Epidemiology, Population & Global Health, School of Cancer Sciences, King’s College London & Guy’s & St.Thomas’ NHS Trust, London

KEYWORDS

Cancer research, Central and Eastern Europe, Central Asia, bibliometrics, European Commission, Framework Programme, Cancer Policy.

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ABSTRACT

Cancer research is an essential part of national cancer control programmes and the emerging economies of Central and Eastern Europe (CEE) and Russian Federation-Central Asia (R-CA) (Commonwealth of Independent States) remain relatively under-studied. Here, we map cancer research activity from the 29 countries across these regions over a ten-year period (2007-16), using a standard scientometric approach. Research activity was compared with the countries' wealth, and with the disease burden from different cancers, and analyses were also performed by research domain (e.g., fundamental cancer biology, surgery). We found that although there was a correlation between outputs and national wealth, there were many outliers, the CEE countries publishing relatively more, and the R-CA less. Outputs reflected cancer burdens but there was a relative paucity of research on lung, colorectal, and gastric as well as pancreatic cancer, as well as research domains such as screening and palliative care. Clinical trials accounted for only 3% of all research outputs from all countries, and were very international, with on average 1.5 CEE countries and 8.0 others involved in each paper, and they were heavily cited (on average, 84 times in five years). Poland was by far the most research active country, but significant needs and opportunities have been identified to expand cancer research activity in all CEE and R-CA countries to enhance national cancer control planning.

INTRODUCTION

Mapping research activity is critical for evidenced-based policy and the development of national cancer control plans [1]. In this analysis, we focus on Central and Eastern Europe (CEE), Russia and Central Asia (R-CA) (Table 1) as their socio-political and science and technology trajectories as well as unmet needs have been very different from those experienced by higher income European countries[2]. Countries that form part of these unique regions have substantially different burdens of cancer, as a proportion of total NCD (Figure 2) as well as different levels of development which require unique policy responses in terms of planning and research systems development[3]. While cancer mortality in Europe has declined steadily [1–4], this trend is not seen in CEE and R-CA where some countries even experienced an increase in cancer mortality[2,4]. This discrepancy has complex background, probably with unequal effects in different countries[4,5]. Causes may include differences in distribution of risk factors, less primary and secondary prevention and consequently higher cancer stage diagnosis, more deadly cancer types, lower access to quality care, fewer available treatment options with lower availability of inovative drugs, shortage of radiotherapy and other equipment, lack of national cancer plans, lack of multidisciplinary teams, absence of comprehensive cancer registries and, as focus of this article, lack of cancer research. [5–7] To date, most of research intelligence and mapping for cancer control has focused on high income countries, and there is a paucity of high resolution comparative data to inform policy-makers at both national and supra-national levels in many emerging powers[6]. Our quantitative analysis builds and expands (geographically) on the detailed and careful *'current situation analysis'* performed by Vrdoljiak and colleagues in 2016 on the state of cancer control and care in CEE and a recent pan European mapping analysis[7]. In light of the rapidly increasing cancer burden across these regions, as well as the need for all these countries to deliver on the ambitious non communicable disease targets for Universal Health Coverage and the Sustainable Development Goals, there is a clear need for more cancer research intelligence to inform policy-makers. Here, we apply well validated scientometric tools to understand the state of cancer research across Central and Eastern Europe, Russia and Central Asia over the last ten years[8,9].

METHODOLOGY

Articles and reviews from 29 countries in CEE and R-CA (Table 1) were identified in the Web of Science (WoS) for the Science Citation Index Expanded and the Proceedings for the 10 calendar years, 2007-16, by means of a complex cancer filter as previously described[10]. This is the most comprehensive global index of cancer publications, however, this does not include non-Indexed country language specific papers. This consisted of lists of 185 specialist cancer journals and 323 title words or phrases with a precision (p, specificity) of 0.95 and a recall (r, sensitivity) of 0.98. The ratio of these two gave its calibration factor = p/r = 0.97. Full bibliographic details of these papers were downloaded to a series of files and converted to an MS Excel spreadsheet by means of a special VBA program (Evaluametrics Ltd).

In order to evaluate the cancer research papers in context, the numbers of biomedical research papers from the countries were also determined for the same years, by means of another complex filter, previously described[11].

The addresses displayed in each of the country's cancer research papers were parsed by a special VBA program to show the fractional contributions of each country to each paper, and also their integer contributions (for example, a paper with two Polish(PL) and three Russian(RU) addresses would be scored 0.4 for PL and 0.6 for RU on a fractional count basis, but 1 each on an integer count basis). The growth rate (annual average percentage growth, AAPG) was only shown for half of the 29 countries (for the others, there was no clear trend with time) on a fractional count basis from a plot of output against time and the best-fit (least squares) exponential trend-line. Country contributions over the decade were also plotted against each country's wealth, as measured by its Gross Domestic Product (GDP), which shows whether countries are publishing more or less than expected from the ratio for other countries in the geopolitical group. They were also plotted against population size, but the correlation is normally much weaker, as was the case here, so the results are not shown. We compared the percentage of each country's overall biomedical research output that cancer research represented in the 2007-16-time period, against the percentage of its total disease burden in DALYs (WHO, 2012) that was due to cancer.

International collaboration is often seen as an important indicator of a country's wider research engagement and a marker of higher impact. This was determined as the percentage of each of the 29 countries' integer count output from within its borders (its fractional count), from other members of CEE and R-CA, and from the rest of the world. A distinction was made between the 11 CEE countries that were EU Member States, those that were CIS members (or associates) and the 6 Balkan countries, in order to see if EU membership had made a difference to collaborative patterns, and data were obtained and compared for two quinquennia, 2007-11 and 2012-16, so as to reveal whether these patterns (in cancer research output) were changing, within each of the three groups.

Two further VBA programs were applied to the database of all papers over this period to evaluate the distribution of cancer papers for 23 different anatomical sites, and in 12 different research domains. These are listed in Table2 and the codes for each anatomical site or research domain are indicated in the Figures and Tables. These "sub-filters" were based on title words and journal name strings.

Another important aspect of cancer research is the publication of the results of clinical trials. Many of these trials are multi-national and the participation of local researchers is often important for the approval of new drugs, or other medical procedures (e.g. innovative surgical or radiotherapy interventions) in particular countries. We searched for clinical trial activity with the following phrases in the titles of the papers: “phase 1/2/3*stud/trial”, “phase I*stud/trial”, “randomis/zed study/trial”, "clinical/controlled trial". Clinical trial activity was further classified by the research domain: drugs (chemotherapy or targeted therapy), surgery or radiotherapy, and by the cancer site.

We also determined the impact of the cancer research papers by means of citation counts in the WoS. We used a standard citation window of five years, beginning with the year of publication of each paper, as a compromise between immediacy and the need to cover the peak year (usually two or three years after the publication year). Thus, we determined the citation counts in the WoS for each country’s papers from 2007-12 (six years). Because they are not distributed normally, we chose three indicators to best capture accurate citation counts, namely arithmetic mean (called actual citation impact, ACI), geometric mean (GCI), and numbers in the top centiles for a group (top 1%, top 2% and top 5%)[12]. The latter are presented as "world-scale" values which are 100 times the ratio of the actual percentage of papers in a given centile to the nominal value[13].Because many papers have zero cites, we add unity to each citation count, determine their geometric mean, and then subtract unity from the result. This is performed by taking the arithmetic mean of the logarithm of the citation counts. This geometric mean is less influenced by the presence of a few very highly cited papers than is the arithmetic mean. All these indicators were determined on the basis of fractional country counts, in order to ensure accuracy, as to attribute the many citations that a multi-national paper may have received to each of the participating countries, some of which may have only made a small contribution, would, we reason, not represent the actual situation.

Mean ACI, GCI and WS values were also determined for the various cancer anatomical site and research domain papers, and for clinical trial papers, but on an integer count basis, as these attributions were not fractionated. The intention was to show whether some types of cancer research attracted more citations than others.

Because of Russia's dominance both in terms of wealth and population, we also made a specific study of two aspects of cancer research in that country. The first to understand the changes in volumes over a much longer time period (1977-2016) and the gender ratio between researchers in these outputs. The methodological approach has been described in detail elsewhere[14]. The second aspect for specific study was the presence of cancer researchers with one or more of 2400 Russian names (ending in "-enko", "-ev", "-nin", and "-ov" and their feminine equivalents) on non-Russian origin papers, to study migration patterns, as previously described[15].

RESULTS

The numbers of cancer papers, on both integer and fractional counts, for the 29 CEE and R-CA countries are shown in Table 3. The integer counts are compared with the countries' biomedical research outputs to give the fraction of the latter that is specifically related tocancer; the fractional counts are used to show the annual average percentage growth, but only for the leading 15 countries, as the annual outputs for the remaining countries were extremely variable, making it very difficult to assign a meaningful growth rate (e-Figure 1, e-Figure 2). The growth rate is highest in the three Baltic states (Estonia, Latvia, Lithuania) and in Romania. It is very low in Bulgaria and Belarus, and actually negative in Croatia (HR). It is interesting to see that the growth is not equcal in all EU Member States, while more or less all Balkan and CA countries, except Serbia and Russia, are lagging behind. Cancer research activity, as a fraction of all biomedical research, varies between zero in Turkmenistan and around 14% in Latvia.

Research outputs tended to correlate better with GDP rather than with population size (**Figure 3**). The correlation, however, is only moderate (r = 0.743), but it does show that there is a huge variation in the volume of cancer research papers compared with national wealth. (When output is plotted against population size, the correlation with the least-squares power law line is much poorer, r = 0.37.) The CEE all publish more cancer research papers than expected, as does Serbia (RS). For example, Serbia publishes more than 240 times as much as Uzbekistan (UZ), although the latter country has a higher GDP.

International collaboration has been increasing steadily over the decade. The amount of international collaboration varied by country; **Figure 4** shows the results based on fractional counts. EU members (blue bars) tend to collaborate more with countries from RoW (yellow bars). For most of the CEE countries, international collaboration has increased in the period between 2012-16 when compared to 2007-11, **see e-Figure 5**, especially in Bosnia & Herzegovina (BA).

Figure 6 shows the correlation between the overall burden from different cancers across all countries (except for Kosovo for which there are no data) and the amount of research that these countries perform on a fractional count basis, expressed as a percentage of all cancer. Belarus is the only country where cancer research exceeds the amount that would be proportional to the cancer disease burden; most other countries only publish of the order of half this amount (dashed line), and Armenia (AM) and Estonia (EE) much less than this.

e-Figure 7 compares the amount of cancer research conducted on each of the main cancer anatomical sites, see Table 2, with the percentage of their burden compared with that from all cancers. Malignant melanoma (MEL), cancers of the central nervous system (CNS) and blood cancers (HAE) dominate relative to other cancers, whereas pancreatic (PAN), gastric (STO) and oesophageal cancers (not shown, values are 2.32, 0.64) are under-represented by a factor of at least two, and for lung cancer (LUN, a major burden in both CEE and R-CA countries) by a factor of more than four.

The research portfolio is dominated by cancer biology (particularly genetics) with over 22% of the total, and pharmaceuticals (chemotherapy plus targeted therapy, 10.5%) (**Figure 8**). There is also a paucity of research on screening and on palliative care. Clinical trials papers numbered 944 in total, and increased slightly from 2.4% of the total in 2007-09 to 3.0% in 2014-16. Almost two thirds of the papers were on drugs (624; 66%). There were relatively few on radiotherapy (82; 8.7%) or on surgery (70; 7.4%). Three cancer sites dominated clinical trials: breast (164 papers, 17.4%), lung (158; 16.7%) and blood (145; 15.4%).

Citation scores for CEE and R-CA cancer papers are presented in Table 4 according to the three measures: arithmetic mean (ACI), geometric mean (GCI) and World-Scale (WS) at three centiles: 1% (164 cites in 5 years), 2% (93 cites) and 5% (47 cites). No country achieved an ACI value equal to or above the mean for the whole group (14.3 cites) on a fractional count basis. The mean ACI values for papers for each cancer site are shown in **e-Figure 9**, and for each research domain (including clinical trials) in **e-Figure 10**. Papers on kidney cancer are the most cited, although they represented only 3% of those with citation scores, as are papers on targeted chemotherapy and ones on clinical trials. These latter papers were very international, with on average 17.0 and 9.6 countries represented respectively.

Because of its economic dominance, we investigated specific aspects of cancer research in the Russian Federation. In 2009-13, overall there were 128 papers concerning clinical trials, and the Russian contribution was 23.4 papers on a fractional count basis. A majority of the papers (n=123, or 96%) acknowledged specific funding, almost all from commercial sources.

We also investigated the location of cancer researchers with Russian surnames. We selected over 2400 Russian names and looked at their research activity (either within Russia or in other countries), e-Figure 11 . The top graph shows a gradual rise in output until 1990, and then a precipitous decline, especially research activity involving men (suggesting a significant migration or cessation of this group), and then a gradual increase, accelerating after 2005 to levels higher than before the end of the USSR. The bottom graph indicates that there were far more male Russian scientists than females conducting cancer research in other countries: the totals include those who were already present in other countries, so clearly there was a major exodus of male Russian scientists particularly after the mid-1990s, and one that continued to accelerate. There were far fewer cancer papers with female Russian scientist names in this period, suggesting that they tended to stay in Russia rather than go abroad.

DISCUSSION

There is significant evidence that in order to improve cancer outcomes, countries need to build their research capacity[16]. Not only does this lead to better patient outcomes through better general cancer knowledge and more rigorous quality and adherence to clinical guidelines, but it also provides evidence to inform national cancer control planning. The countries in our analysis situated in Central and Eastern Europe and Central Asia all have unique and complex historical, political, economic and health trajectories. Furthermore, their therapeutic geographies are complicated, with significant inequalities, refugees, ethnic minorities, migration patterns, and rurality, and their relative dimensions of socio-development are uneven, from Russia at a population of over 143M `and a GDP of 3.6 trillion USD to Montenegro at around 1M population and a GDP of around 8 billion. These regions are all experiencing increasing cancer burden as they move through their respective demographic, epidemiological and development transitions[17].

Despite issues around the completeness of the registration of cancer cases, it is clear that increasing prosperity (GDP/capita) for the countries in our study is aligned with increasing cancer burden. For both CEE and CIS countries, the importance of prevention and public health for reducing such trajectories is crucial. However, our analysis shows that these are among the most poorly researched areas across all research domains. More in-depth cancer site-specific analysis shows remarkable similarities between the countries with lung, colon, rectal, breast and gastric dominating the cancer landscape. Taken together, haemato-oncological cancers also pose a significant burden. The high burden of colorectal, and gastric (particularly in CIS countries) again points to the importance of public health e.g. (eradication of *H pylori* for gastric cancer) and screening (coupled with efficient multi-modal treatment) for colo-rectal cancer. However, both public health and screening are orphan areas of research across all countries. Furthermore, considering the burden of colorectal, lung and gastric cancer, the research dedicated to these site-specific malignancies falls seriously short of what is required. It must be noted that both in CEE and CIS countries, evidence-based health policies are the exception rather than the rule. Generally, medical (and general science) research priorities are not determined by the local or national needs, but imposed by the European or international financing organizations. There is also significant focus in research on both cancer biology discovery, as well as research on cancer drugs (which includes biomarker, chemotherapy and targeted therapy); biomarker and chemotherapy outputs when added to the former make up nearly 40% of total domain-specific research activities. Palliative care, screening and radiation oncology all are significantly below the percentages we see in other comparable EU countries. However, it is clear that international clinical trials, particularly those involving new molecular targeted therapies dominate the research landscape (20% of overall research outputs across CEE and R-CA). These findings reinforce the need for more properly designed, country-or-region specific studies, with socio-economic models to help inform prioritisation of therapeutic interventions, help manage introduction of new technologies (medicines, surgery, radiotherapy) and deliver affordable and equitable care and better outcomes. The lack of epidemiological research is also in a large part due to the lack of high quality cancer registries[5,18], a key policy recommendation from previous analysis[19]. It is also clear from this previous policy analysis that if many of the recommendations for improving care are to be realised both in CEE and R-CA (e.g. screening programs, development of clinical guidelines, pharmacoeconomic evaluations, allocative efficacy for cancer budgets, and nationwide prevention programmes) then (sub)region-specific data is going to be required, and this can only be achieved through significant enhancement of research activities in these domains, which would also drive more affordable innovation in cancer[20].

Many CEE have performed well in delivering research outputs commensurate or above what would be expected for their respective wealth, especially Poland. CIS countries, however, have fallen behind, especially Kazakhstan and Russia. However, despite the significant research activity of Poland, it's international impact (measure by world scale values) remains modest with Czech Republic and Hungary performing better. This phenomenon is particularly striking for those CEE countries with a high annual publication growth rate (the Baltic states and Romania) but a limited international impact. One possible explanation is the nature and impact of national legislations with regards to academic advancement. For example, in Romania it is mandatory to have a certain number of scientific publications in order to get an academic promotion but the quality and thei impact factor of these journals are not leading criteria.Furthermore, despite significant bilateral Science and Technology (S&T) agreements between CEE and Central Asian CIS countries, this has not translated into joint cancer research programmes. Our analysis suggests that a number of countries in CEE and, in the future, R-CA could and should be leading more international cancer studies and trials[21].The growing internationalisation of cancer research from Central Asia is, in part, due to wider, often generic co-operation and partnership agreements, such as the 719 million euro Development Co-operation Agreement (from 2007 to 2013). Our analysis has also identified other anomalous areas that warrant further country-specific investigation. Kazakhstan for example, with an R&D expenditure as a % of GDP of nearly 0.2%, but with 424 self-declared research organisations with over 17,000 personnel, clearly has significant potential to rapidly increase its cancer research activities.

International collaboration is remarkably heterogeneous. However, two crucial trends come out of our analysis. The first is that Russia as well as other CA countries remains relatively introspective, with most research conducted within national borders. Despite this, Russian cancer researchers have retained an impressive impact, with a world scale value rivalled only by the Czech Republic (Ukraine is a major outlier because of size). The second trend we have uncovered is that CEE countries broadly direct their international collaborations towards the EU, a trend that has almost certainly been driven by EU Framework research funding programmes, thus showing the impact of a pan-European research funding policy. The overall trend across all countries is a moderate increase in internationally collaborative research activities. In no case has a country gone backwards. The importance of internationalisation in Research and Development has been hypothesised for some time,[22] but it has only become apparent relatively recently how crucial internationalisation can be for research systems development and the current study adds to this body of evidence . Internationalisation in R&D drives quality and excellence, market share, cost optimisation and wider science diplomacy. Our analysis shows that CEE countries that were part of the EU benefited from European Commission programmes, starting with 4th Framework Program (FP) with utilisation of the two main schemes for stimulating research between CEE and the wider EU – PECO and COPERNICUS. However, from a cancer research perspective, we found little impact of the collaboration programmes set up in the mid 1990's to engage wider Central Asia e.g. International Association for Cooperation with Scientists from the former Soviet Union (INTAS). This may have been in part due to the premature ending of this programme in early 2000, with the policy re-orientation of the EU in FP6 and 7, and a lack of success of Central Asian partners in winning programmatic funding[23]. The Russian

Federation, however, did have the highest rate of participation as a ‘third country’ up to and including the EU’s Framework 7 programming. Yet, this seems to have had only a modest impact in the cancer research domain.

Our in-depth analysis of Russian Federation cancer researchers found that the gender gap that developed in the 1980’s between male and female researchers did close, although there were indications that this was starting to widen once more as outputs grew from the mid 2000’s. More worryingly for Russian cancer research, there was significant numbers of Russian researchers appearing on cancer research outputs from other countries, a trend that has been, and continues, to grow since the late 1980’s, irrespective of international engagement, and bilateral international collaboration agreements around discovery science . At present, the Russian Federation is undergoing significant changes in the fight against cancer. At the national level, a national strategy for combating cancer is being developed, it should be submitted by the Russian government in 2018. A network of national medical centers for the research and treatment of cancer, including of pediatric cancer, has been implemented since 2016, a program of government support for independent research in the field of oncology.

In developing their cancer research systems, it is clear that many of the low and lower middle-income countries from this group e.g. Uzbekistan and Tajikistan, do not have the fiscal headroom at present to establish effective cancer research programmes. Instead, the priorities for these countries must be to build basic health systems as well as some form of science and technology base. More broadly, the regional development priorities have been economic and industrial, and not health or research, particularly in Central Asia. There are clearly opportunities for more regional co-operation in both general and cancer-specific research, building on the Eurasian Economic Commission and the Economic Cooperation Organisation. Technical co-operation in science (amongst other areas) is already part of the United Nations Industrial Development Organisation mandate, and this almost doubled since 2012[24]. However, an analysis of expenditure reveals the majority of resources being earmarked for energy, poverty reduction, and trade capacity building. There is clearly an urgent need to revisit this to accelerate not only cancer but overall NCD control[25]. Platforms already exist, and could be utilised for cancer research, for regional and global outreach, and high-level missions between and outside CEE and R-CA, focusing on cancer and NCD research capacity building could pay dividends. For example, over the last 5 years the US-Polish Cancer Research group have provided a platform for cancer planning for care and research with international partners. A strategy of 'cancer research inclusion' by the EU and USA, for example by funding research partnerships between major cancer centres[26], could also help bridge and develop relationships for wider research system reforms, building on existing institutional partnerships within and outside the regions[27].

Finally, it is clear from empirical work around expenditures and mortality-incidence ratios that country specific funding for public sector cancer control, including cancer research, is too low (even for the stage of development for each country)[28]. These deficits cannot be 'made up' from external collaborations or resources[29], neither can they be expected to 'trickle down' from general S&T funding or substituted by the private sector. There is a critical need to find the fiscal headroom to support our policy recommendations for funding cancer research of public value,[30]which will have significant national and international impact[31].

Policy Recommendations for Cancer Research Systems (Pull out box in main text)

1. Adjust and / or implement national cancer research policy strategies as part of wider National Cancer Control Plan reforms.
2. Strengthen human resources for cancer research, particularly in clinical research, and in domains such as surgery and palliative care
3. Strengthen therole of public sector funding both nationally, and through collaborations, internationally. Create within this framework, clear national cancer research policy needs for engagement with the private sector
4. Build better (sub)regional co-operation, both in cancer research capacity and capability training and in the creation of more resources for research teams
5. Establishment of national cancer medical centers for the research and treatment integrated into a joint network.

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Table 1. List of CEE (Central &Eastern European) countries, with ISO2 codes; group (BALK = Balkan countries, CIS = Members or associates of Commonwealth of Independent States, EU = European Union Member States); Gross Domestic Product in 2011 (USD, billion); and population in 2009, million.

Country	*ISO2*	*Group*	*GDP*	*Pop'n*	*Country*	*ISO2*	*Group*	*GDP*	*Pop'n*
Albania	AL	BALK	12.8	3.6	Lithuania	LT	EU	42.7	3.6
Armenia	AM	CIS	10.1	3.0	Montenegro	ME	BALK	4.5	0.7
Azerbaijan	AZ	CIS	62.3	8.2	Poland	PL	EU	514	38.5
Belarus	BY	CIS	55.5	9.6	Moldova	MD	CIS	7.0	4.3
Bosnia &Herz.	BA	BALK	18.0	4.6	Romania	RO	EU	190	22.2
Bulgaria	BG	EU	53.5	7.2	Russia	RU	CIS	1850	140
Croatia	HR	EU	63.8	4.5	Serbia	RS	BALK	45.1	7.4
Czech Republic	CZ	EU	215	10.2	Slovakia	SK	EU	96.1	5.5
Estonia	EE	EU	22.2	1.3	Slovenia	SI	EU	49.6	2.0
Georgia	GE	CIS	14.3	4.6	Tajikistan	TJ	CIS	6.5	7.3
Hungary	HU	EU	140	9.9	Macedonia	MK	BALK	10.3	2.1
Kazakhstan	KZ	CIS	178	15.4	Turkmenistan	TM	CIS	25.7	4.9
Kosovo	XK	BALK	6.5	1.8	Ukraine	UA	CIS	165	45.7
Kyrgyzstan	KG	CIS	5.9	5.4	Uzbekistan	UZ	CIS	45.4	27.6
Latvia	LV	EU	28.3	2.2					

Table 2. List of sites to which cancer research papers could be assigned, with trigraph codes, and of domains, with tetragraph codes.

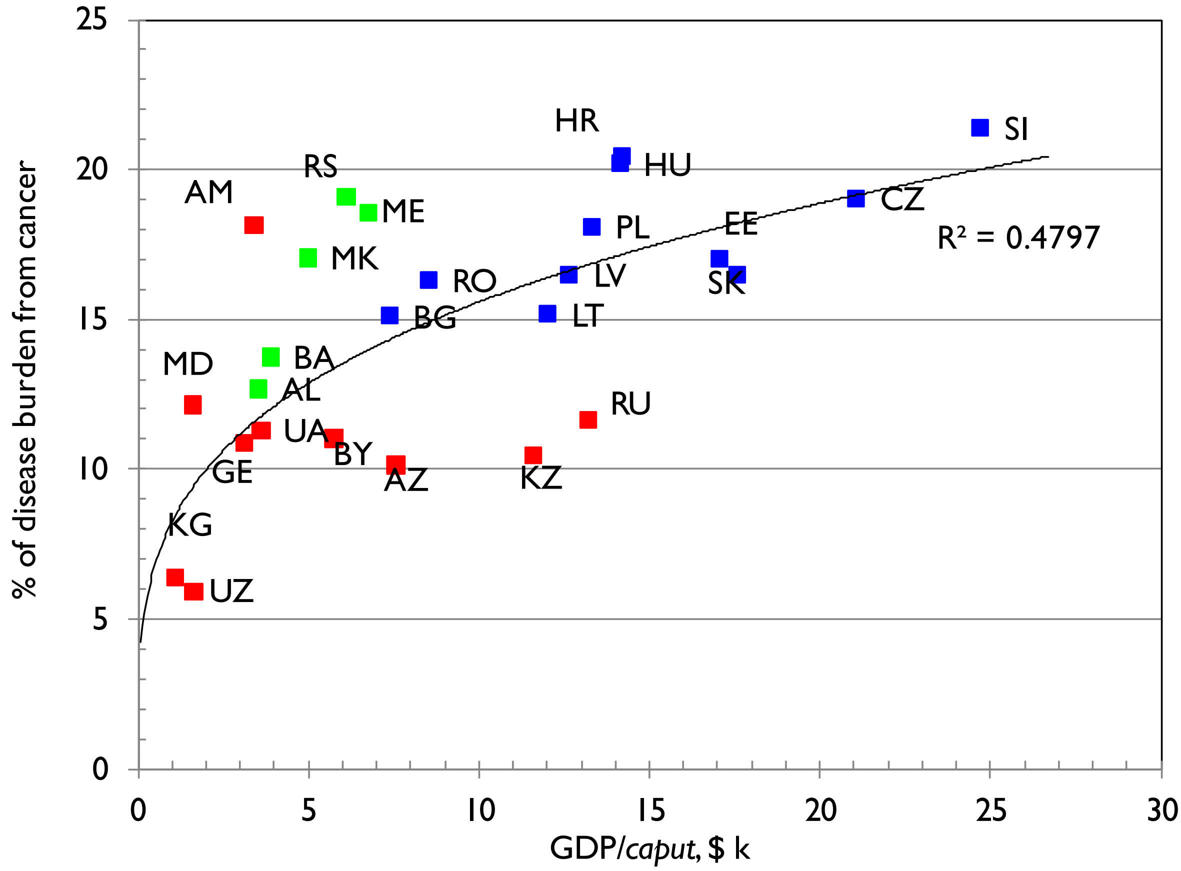
Manifestation	*Code*	*Manifestation*	*Code*		*Research domain*	*Code*
Bladder	BLA	Breast	MAM		Cytotoxic CXT	CHEM
Bone	BON	Melanoma/skin	MEL		Diagnosis	DIAG
Cervix	CER	Oesophagus	OES		Epidemiology	EPID
Central nervous system	CNS	Ovaries	OVA		Cancer Biology	GENE
Colon / Rectum	COL	Pancreas	PAN		Palliative Care	PALL
Gallbladder	GAL	Prostate	PRO		Pathology	PATH
Haematological	HAE	Stomach	STO		Prognosis	PROG
Head & Neck/Mouth	HEN	Testicles	TES		Quality of Life	QUAL
Kidney	KID	Thyroid	THY		Radiotherapy	RADI
Liver	LIV	Uterus	UTE		Screening	SCRE
Lung, Trachea, Bronchus	LUN	Vulva	VUL		Surgery	SURG
Lymphoma	LYM				Targeted therapy	TARG

Table 3. Outputs of biomedical (BIOM) and oncology (ONCOL) research papers, 2007-16, from 29 CEE/CIS RF countries (for codes, see Table 1), with percentage of biomedical research on cancer, and annual average percentage growth (AAPG) for the leading 15 countries.

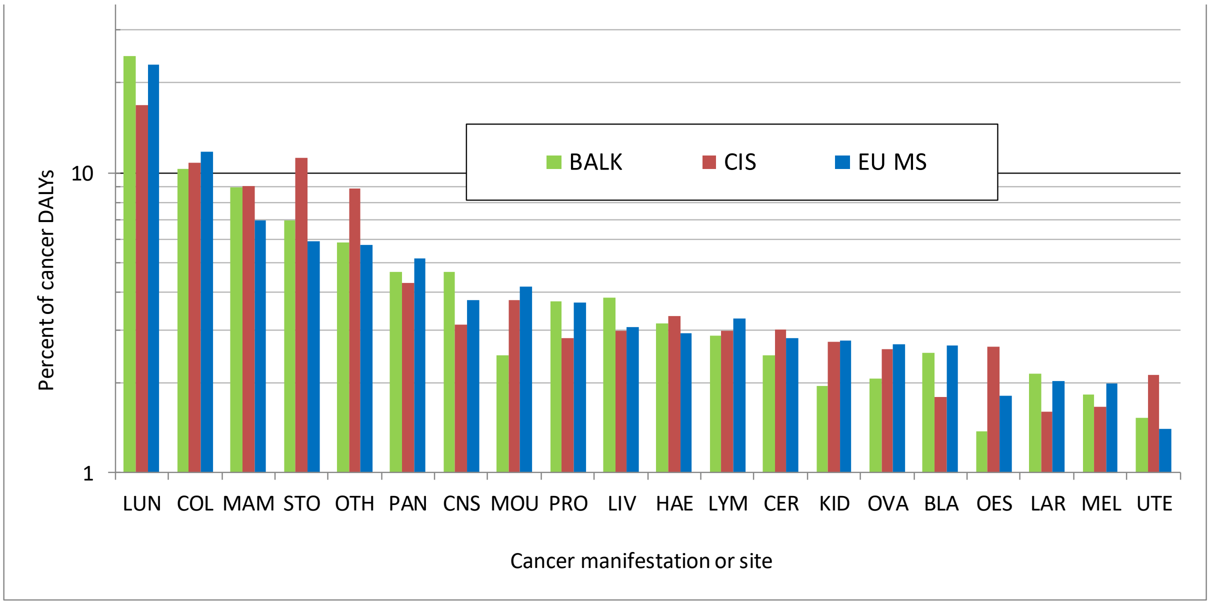
ISO2	*BIOM*	*ONCOL*		*% BM*	*AAPG*		*ISO2*	*BIOM*	*ONCOL*		*% BM*
	INT	*INT*	*FRAC*	*INT*	*FRAC*			*INT*	*INT*	*FRAC*	*INT*
PL	91612	11585	8860	12.6	6.7		BA	2118	243	137	11.5
CZ	44671	5352	3421	12.0	5.5		KZ	1099	98.0	50.9	8.9
RU	55620	4077	2744	7.3	7.5		MK	1289	95.0	62.7	7.4
HU	29324	3085	1910	10.5	5.1		AM	1687	73.0	45.9	4.3
RO	22833	2875	2116	12.6	15.0		GE	1594	61.0	27.7	3.8
RS	18323	2299	1853	12.5	7.0		AL	589	45.0	23.3	7.6
SI	13788	1546	1003	11.2	4.7		ME	509	43.0	22.2	8.4
HR	14760	1481	1115	10.0	-0.9		MD	518	39.0	18.6	7.5
SK	12166	1304	803	10.7	5.6		UZ	527	22.0	7.56	4.2
BG	8979	776	512	8.6	0.6		AZ	481	18.0	6.45	3.7
UA	7587	637	298	8.4	8.6		KG	267	14.0	4.91	5.2
LT	6324	575	393	9.1	14.0		XK	100	5.00	3.17	5.0
BY	2223	255	98.8	11.5	2.6		TJ	100	2.00	0.71	2.0
LV	1848	255	113	13.8	15.2		TM	9	0	0	0.0
EE	5646	253	111	4.5	13.1		**EEU**	**324937**	**33641**	**25762**	**10.4**

Table 4. Mean five-year citation scores (ACI, arithmetic mean, and GCI, geometric mean) for 16 leading CEE/CIS countries (with at least 90 citable papers), and numbers in top centiles and mean world-scale value; all based on fractional counts of countries. *Countries ranked by mean world-scale value. ISO country codes in Table 1 .*

	ACI	*GCI*	*top1%*	*top 2%*	*top 5%*	*WS 1%*	*WS 2%*	*WS 5%*	*Mean WS*
Cites:			*164*	*93*	*47*				
UA	13.2	3.5	1.6	3.5	6.8	107	119	92	106.0
RU	7.7	2.3	5.4	10.8	30.1	40	40	44	41.4
CZ	11.4	6.0	4.8	13.3	55.2	26	36	60	40.6
HU	10.3	5.2	2.0	6.9	22.7	20	34	45	33.1
EE	10.8	6.0	0.2	0.2	1.0	35	17	42	31.2
PL	8.0	3.5	10.7	21.6	77.7	23	23	34	26.8
SI	8.7	4.4	0.3	2.3	15.5	4	20	54	26.1
LT	6.1	2.9	0.4	0.7	2.5	20	19	28	22.6
LV	7.8	4.1	0.1	0.2	0.8	13	20	32	21.8
SK	8.0	4.0	0.4	1.0	8.2	9	12	38	19.5
HR	6.2	2.9	0.9	2.4	7.7	13	17	22	17.4
RO	5.5	2.6	1.2	2.1	9.5	12	11	20	14.1
BY	6.8	3.0	0.0	0.0	0.9	2	3	33	12.6
RS	5.1	2.5	1.4	1.9	6.9	14	10	14	12.3
BG	6.0	3.0	0.2	0.4	1.8	7	7	12	8.7
BA	2.9	1.2	0.0	0.1	0.4	2	5	8	5.0



e-Figure 1. Plot of the percentage disease burden from cancer in 2012 (in DALYs) compared with the wealth of EEU countries (2011, thousand US dollars, per head). *Country codes in Table 1.*



e-Figure 2. Burden of different cancers in three groups of EEU countries, 2010. BALK = five Balkan countries; CIS = 12 members of the Commonwealth of Independent States; EU MS = 11 European Union Member States. *For site codes, see Table 2.*

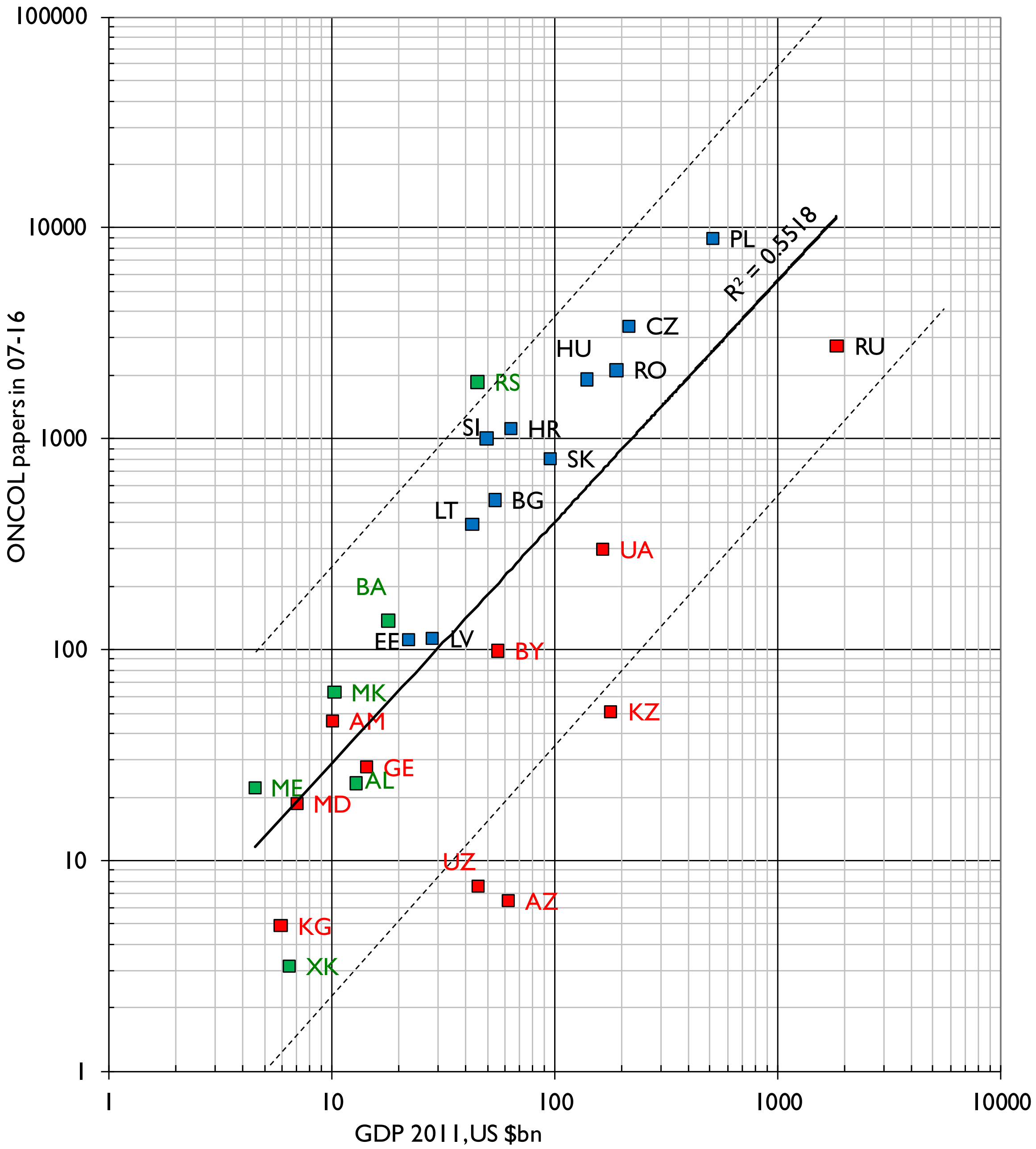


Figure 3. Relationship between cancer research papers in 2007-16 and GDP in 2011 for EEU countries. *CIS countries marked red; EU Member States marked blue; Baltic states marked green. Grey lines above and below black trend-line show outputs x 10 and x 0.1. Country codes in Table 1.*

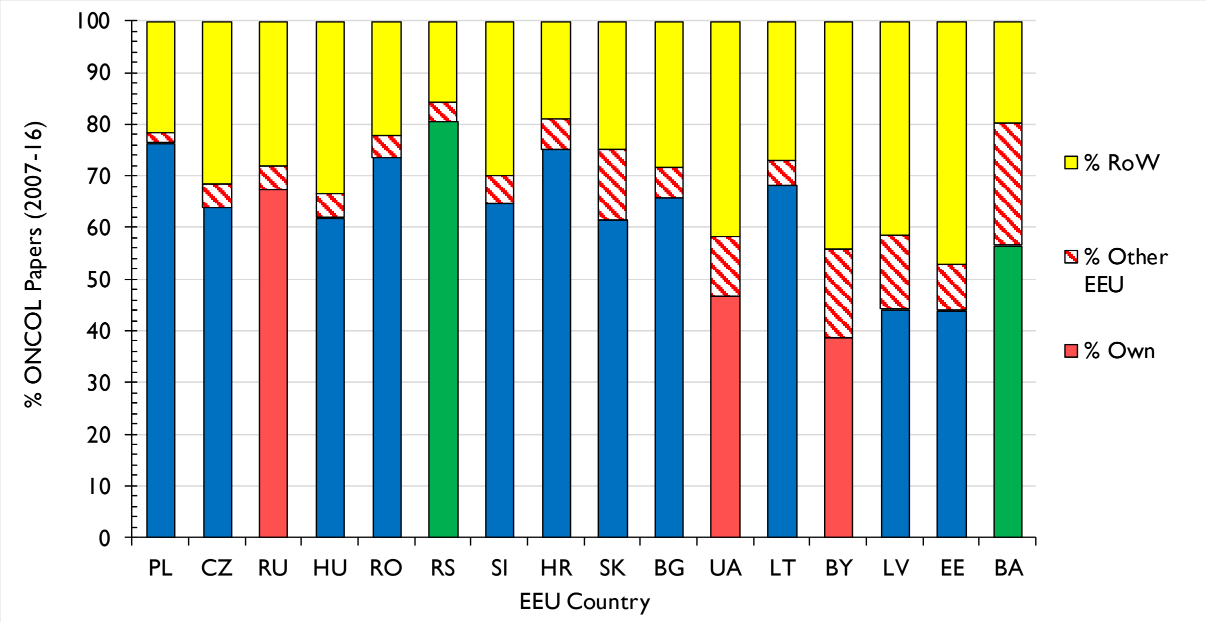
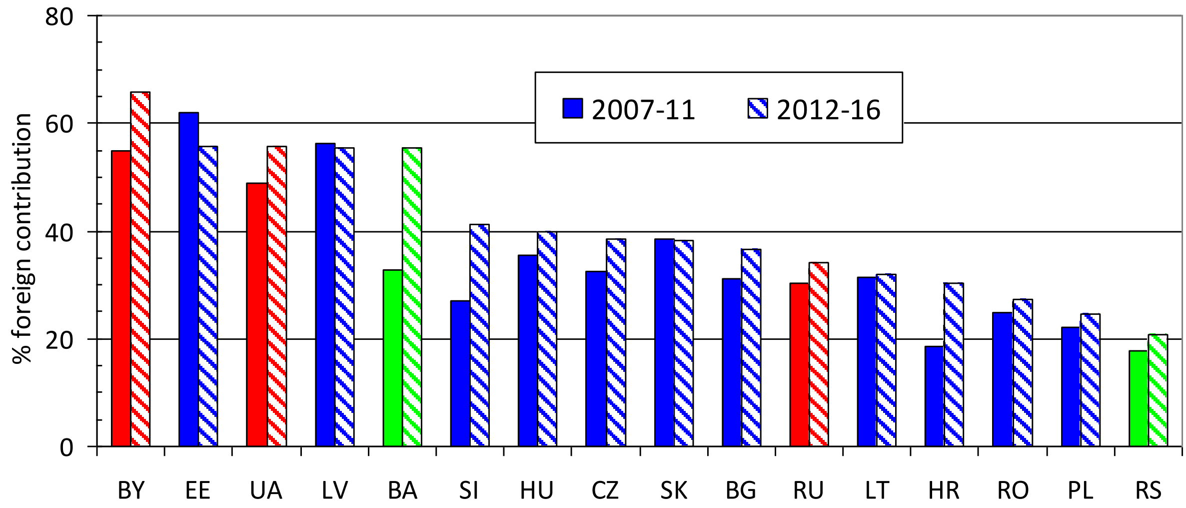


Figure 4. Extent of international collaboration for 16 leading EEU countries in cancer research, 2007-16. *Countries ranked by numbers of papers; blue bars: EU MS; red bars: CIS countries; green bars: Balkan countries. Fractional country counts; for codes see Table 1.*



e-Figure 5. Extent of international collaboration for the 16 leading countries in two five-year periods. *Country codes as in Table 1*.

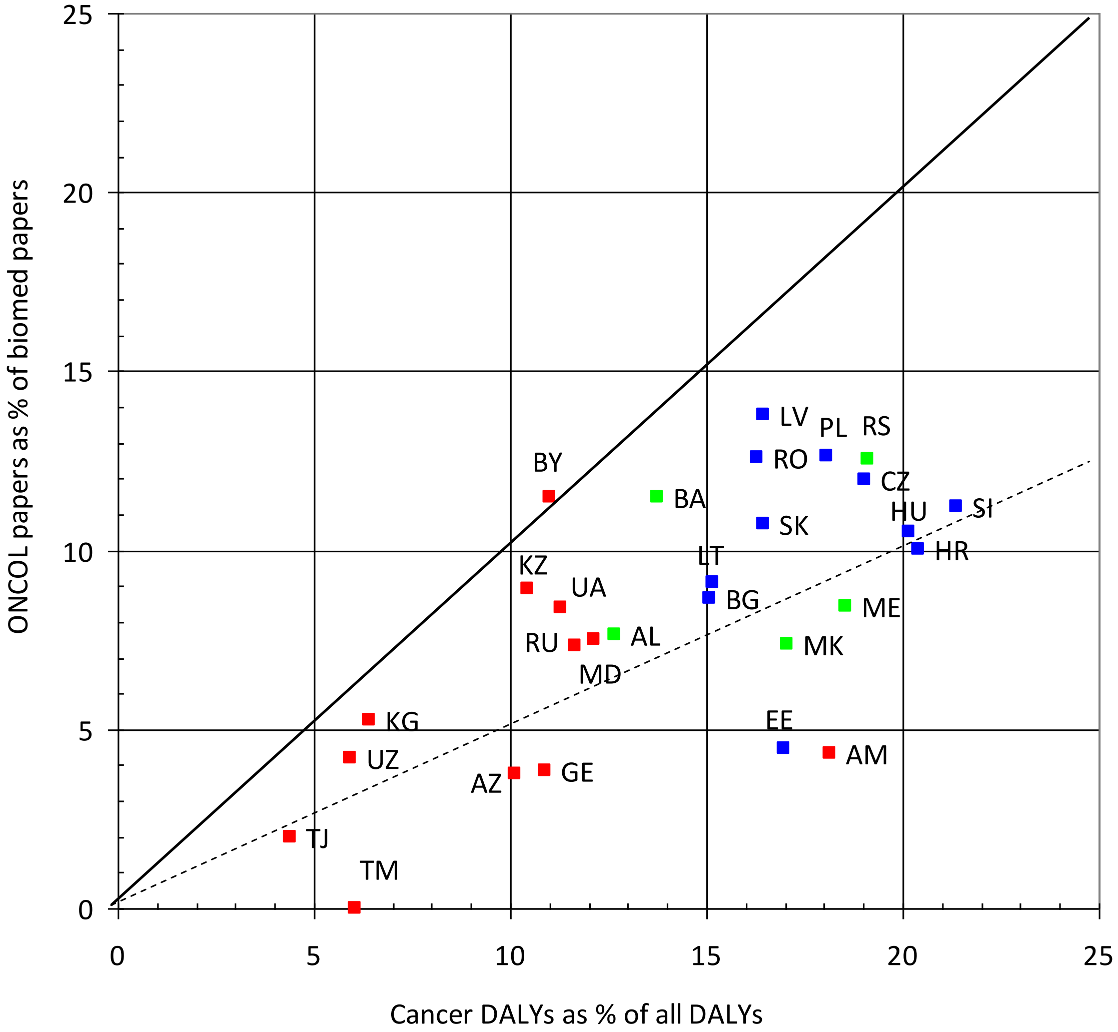
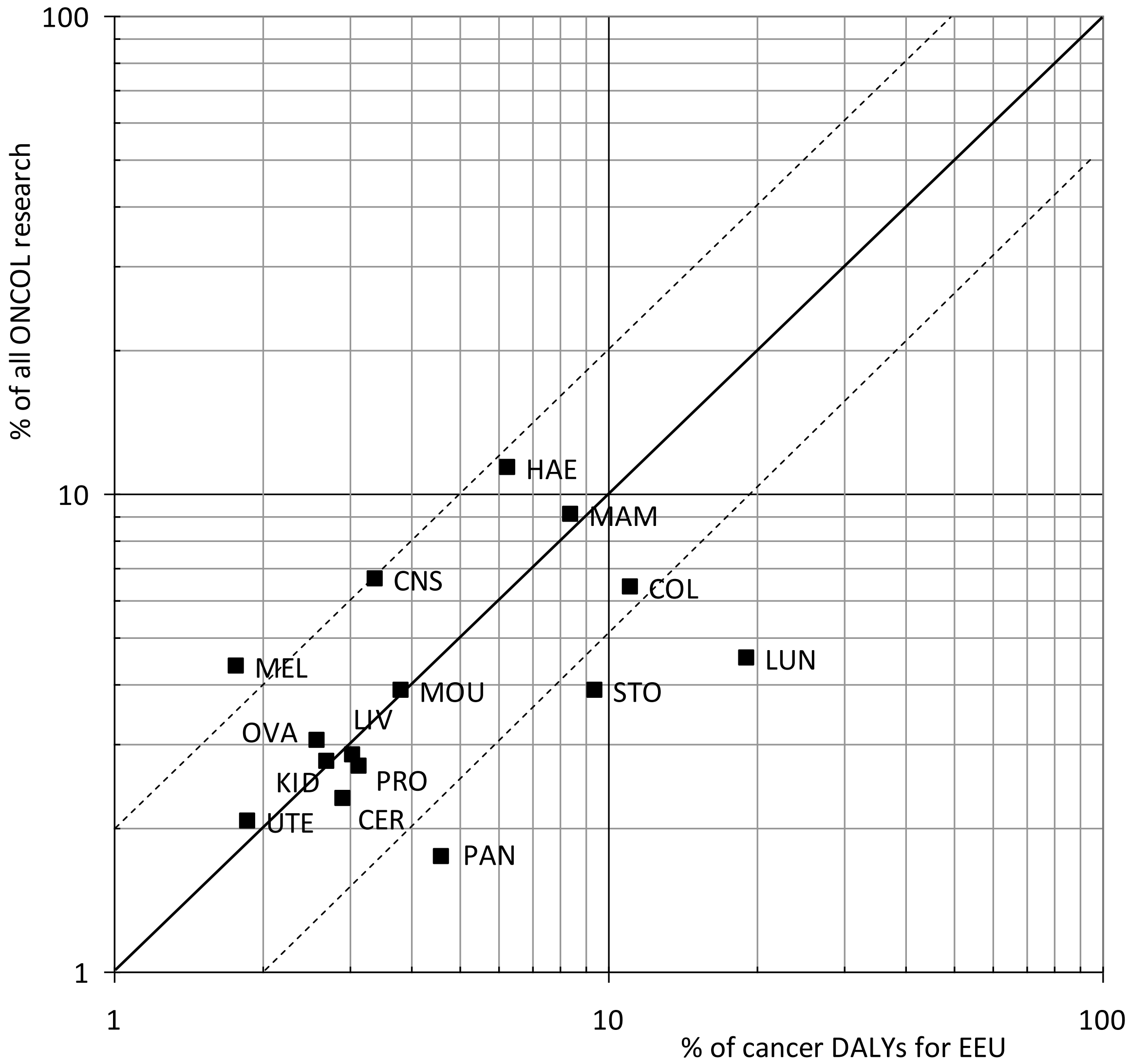


Figure 6. Scatter plot showing relationship between relative burden from cancer in 2012 (abscissa) and percentage of biomedical research papers that are on cancer, 2007-16, for 28 EEU countries (Kosovo not shown). *EU Member States: blue squares; CIS states: red squares; Balkan states: green squares. For country codes, see Table 1. Dashed line shows where research outputs are only half of percentages corresponding to burden.*



e-Figure 7. The amount of research from the EEU countries, 2007-16, as a function of the disease burden from different cancers, 2010. *Site codes in Table 2. Diagonal lines show equivalent percentages, and ones that are x 2 or x 0.5 of the relevant burden*.

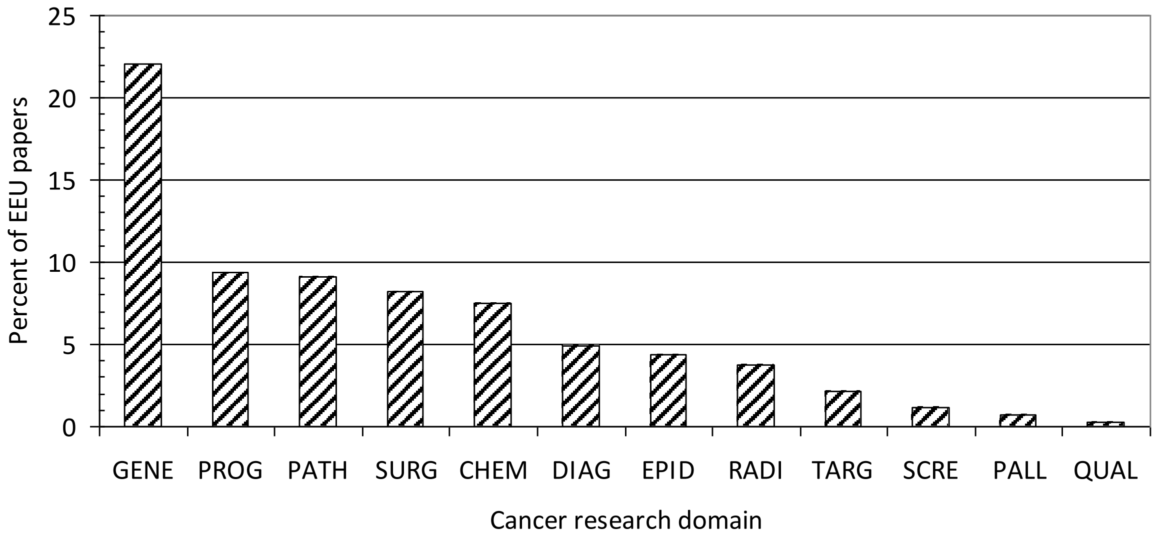
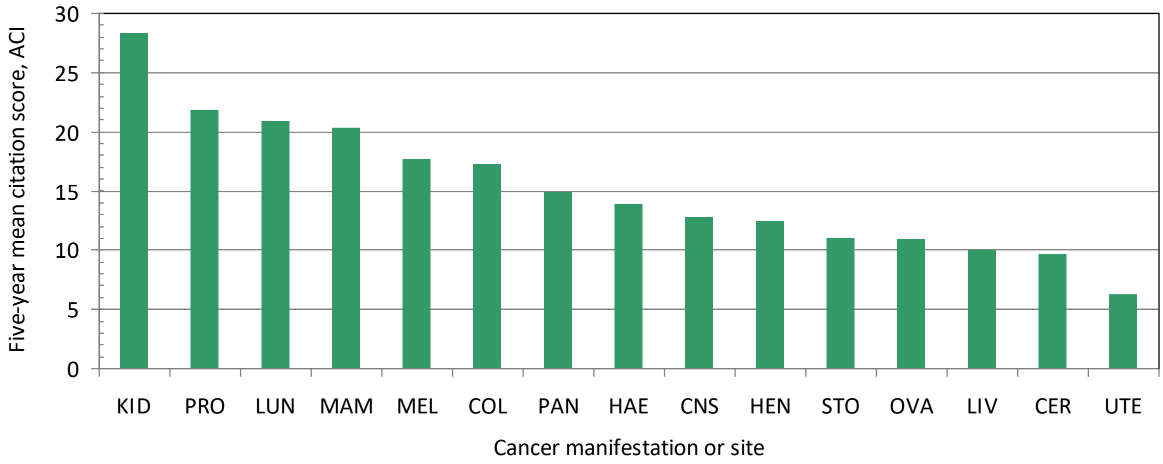
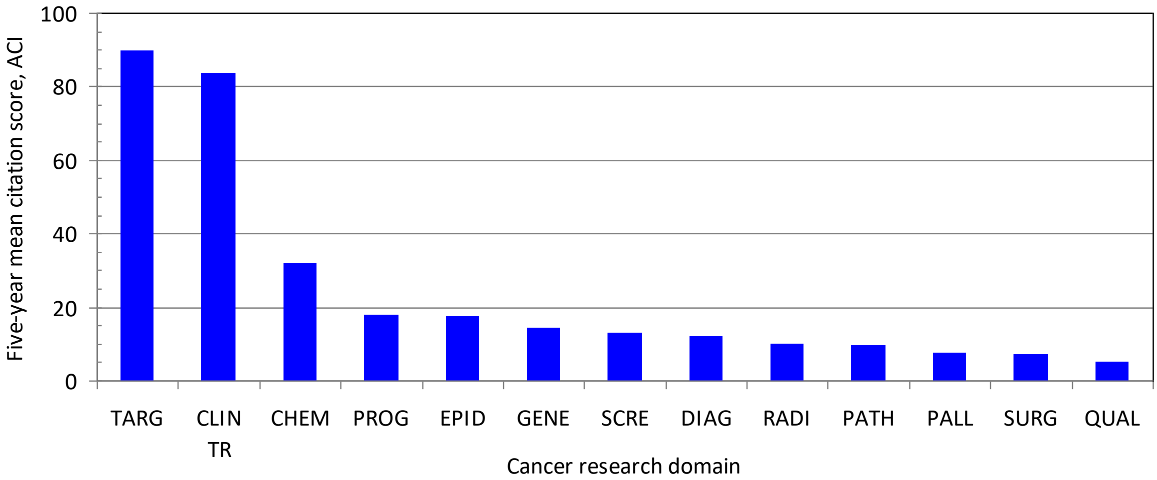


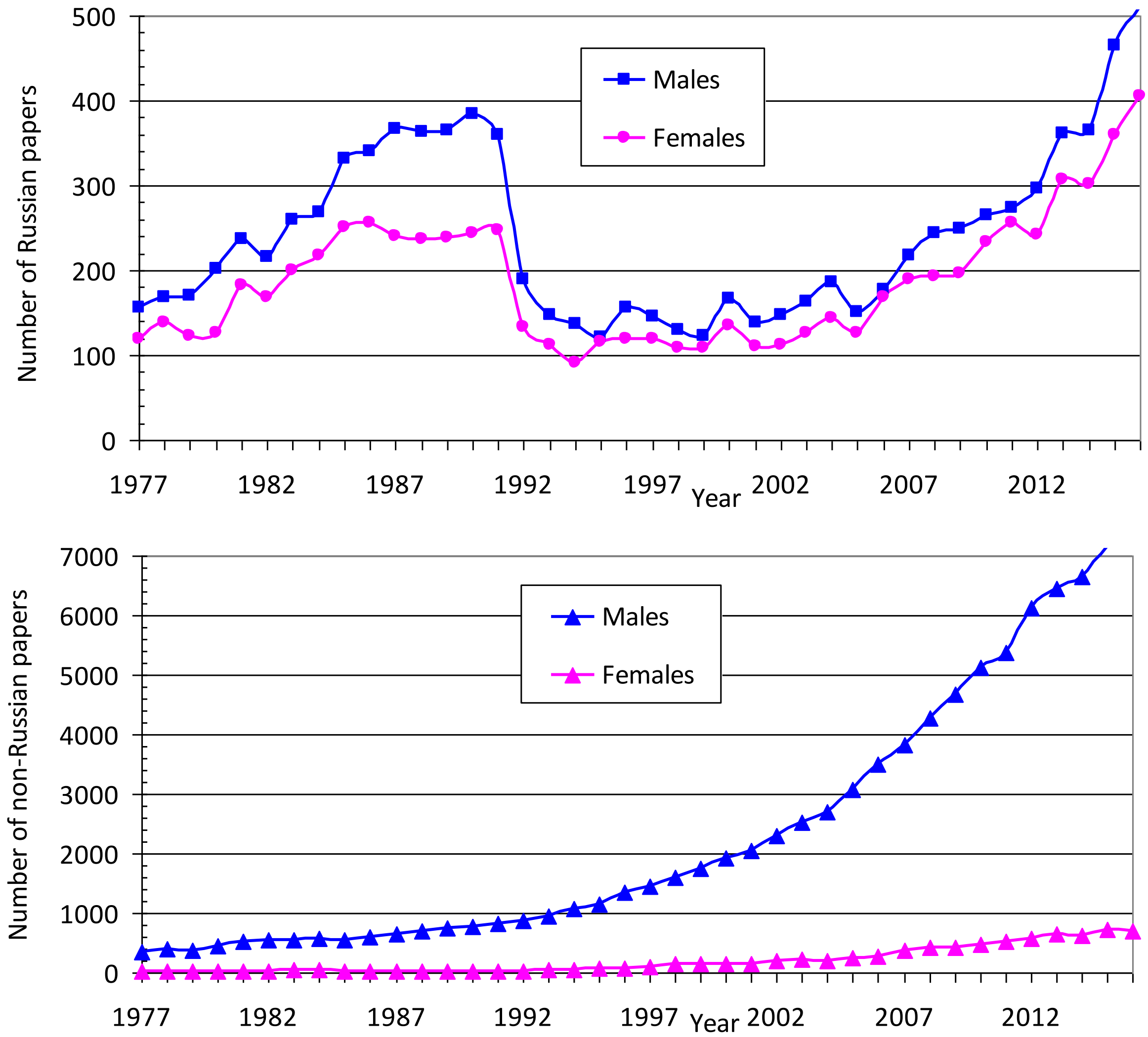
Figure 8. Partition of EEU cancer research papers by domain, 2007-16. *For codes, see Table 2.*



e-Figure 9. Citation scores of EEU cancer papers on different sites. *For codes, see Table 2.*



e-Figure 10. Citation scores of EEU cancer papers in different research domains. *For codes, see Table 2. CLIN TR = clinical trials*



e-Figure 11. The presence of scientists with one or more of over 2400 Russian names on papers from 1977-2016 in Russia (top graph) and in other countries (bottom graph; note different scale).

Figure Legends

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